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EXAMINER	
KRASS, FREDERICK F	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Supplementary Action

While preparing a supplemental examiner's answer in commonly assigned USSN 09/143,572, the examiner realized he had inadvertently omitted repeating the new matter rejection made there in the instant case. Given the similarities between the two cases and the corollary desire for consistency engendered by same, the examiner has chosen to issue a supplemental action in this case. The new action is the same as the previous action, except for inclusion of 1) a "New Matter Rejection" and 2) some additional commentary on "Omnibus" claims in the "Indefiniteness" section.

New Matter Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 7-9 and 13-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain newly introduced subject matter which was not described in the specification as originally filed in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the newly added subject matter.

There is no support in the specification as originally filed for the claimed limitations that the CSAID compounds be "[invented/disclosed/used] after/before the priority date of March 26, 1996". The provisos clearly introduce new concepts to the claims. Priority dates show when a particular inventor invented his or her own claimed subject matter; it is quite a stretch to assert that priority dates can be used to support the concept of someone else's prior art not being "invented", "disclosed" or "used" after a certain date.

Written Description Rejection

Claims 1-4, 7-9 and 13-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification sets forth assays for screening compounds to identify those that purportedly inhibit the "production, transcription, translation or activity" of 14 kDa PLA_2, and methods of treating diseases characterized by "excessive, undesired or inappropriate angiogenesis" using such compounds. Nowhere, however, does it specify which particular compounds have the desired characteristic of selectively inhibiting which particular mechanisms (production, transcription, translation or activity) of 14 kDa PLA_2 action, other than those having the general formulae set forth at page 5 of the specification, which are apparently able to generally inhibit the activity of that enzyme in some unidentified way.

The appearance of mere indistinct words (here the word "inhibitor") in a specification or a claim, even an original claim, does not necessarily satisfy the written description requirement. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004). A description of what a material does, rather than of what it is, usually does not suffice to provide an adequate written description of the invention. Univ. of Cal. v. Eli Lilly, 119 F.3d 1559, 1568 (Fed. Cir. 1997). Furthermore, to the extent that a functional description can meet the requirement for an adequate written description, it can do so only in accordance with PTO guidelines stating that the requirement can be met by disclosing "sufficiently detailed, relevant identifying characteristics," including "functional characteristics when coupled with a known or disclosed correlation between function and structure." Univ. of Rochester v. G.D. Searle, 68 USPQ2d 1424, 1432 (DC WNY 2003). No such correlation has been disclosed here; at best all that can be inferred from the instant specification is that compounds having the general formulae set forth at page 5 of the specification inhibit the production of downstream products of 14 kD PLA2, such as arachidonic acid. See the first paragraph on page 13. Whether this was specifically due to inhibition of enzyme activity, or also due inhibition of production, transcription or translation, or some combination of these, is not clear from the data presented.

The examiner recognizes that the fact situation in the Rochester cases was extreme, with Applicant disclosing there no (or possibly one) specific compounds. The reasoning provided by the court can be fairly extended to less extreme situations (*i.e.*, where a limited number of species is actually disclosed, such as here), however, given the court's recognition that:

> [I]n claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can

> distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. Rochester (2003) at 1431.

As was the case in Rochester, there is no such specificity here, nor could one skilled in the art identify any particular compound, other than those having the general formula set forth at the top of page 5 of the specification, as being able to inhibit any particular mechanism of 14 kDa PLA_2 action, other than to inhibit its "activity" in some unspecified way.

Scope of Enablement Rejection

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of airpouch granuloma in mice, does not reasonably provide enablement for the treatment of diseases characterized by "excessive, undesired or inappropriate angiogenesis" generally, nor other specific conditions, *e.g.* atherosclerosis, tumor metastasis, *etc.* in mice, let alone human patients. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in

which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to the treatment of chronic diseases characterized by aberrant

[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

angiogenesis in mammals requiring such treatment. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites Gupta et al., *Postgrad. Med. J.*, vol. 81, pp. 236-242 (2005).

That article plainly demonstrates that the art of antiangiogenesis therapy is very unpredictable. As discussed at the righthand column of page 239, one major problem resides in the lack of any reliable correlation between the rodent models generally used (such as by Applicant), and the much more complex therapeutic situation involved with humans. Moreover, treatment for each type of disease state (tumor metastasis, ocular angiogenesis, cardiovascular diseases, *etc.*) is unpredictable as well and is dependent on the specific mechanisms and therapeutic markers peculiar to each. Indeed, the reference recognizes that it is not yet even feasible to monitor the antioangiogenic response in human patients, let alone develop individualized therapies for each disorder based on a general animal model.

The situation is even more complex in the case of tumor metastasis, a notoriously unpredictable condition. Therapies targeted to the common mechanism of angiogenesis have been tried as a means to overcoming the problems arising from the tremendous heterogeneity among different cancer types. Antiangiogenic therapies remain unpredictable, however, and have mainly failed due to numerous factors, including the tissue and/or tumor specific nature of vasculature. Due to such inherent difficulties, additional markers associated with specific pathologies must further be identified, and even when they are no reasonable expectation of therapeutic success can be guaranteed (in part because drug delivery to the ischaemic site can be a major limiting factor, especially given the lack of tools with which to monitor site specific drug

availability within the tumor). See Gupta et al. at the passage bridging the bottom of the lefthand column to the penultimate line on page 239. As a result, different types of cancers must follow individualized strategies for angiogenesis based treatment. Consequently, most "treatments hold promise but will have to be clinically tested for different kinds and different stages of tumor growth." Gupta et al at the lefthand column of page 240.

Clearly then, the treatment of diseases characterized by aberrant angiogenesis, particularly in humans, is extremely unpredictable, particularly in the case of tumor metastasis.

2. The breadth of the claims

The claims vary in breath, some (such as claim 1) very broadly reciting the treatment of diseases "characterized by excessive, undesired or inappropriate angiogenesis", others (such as claim 7) reciting the treatment of specific conditions such as diabetic retinopathy. All, however, are extremely broad insofar as they disclose the treatment of any type of mammal, including humans.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for determining the particular administrative regimes (dosages, timing, administrative routes, *etc.*) necessary to treat all the various diseases claimed, particularly in humans. The working examples are limited to only a specific animal model, the murine air pouch granuloma model. Thus Applicant has at best

provided specific direction or guidance only for the treatment of air pouch granuloma in mice. No reasonably specific guidance is provided concerning useful therapeutic protocols for any other diseases in mice, let alone in humans.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably used as antioangiogenic agents as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Indefiniteness Rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 7-9 and 13-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant provisos reciting "wherein the compounds were [invented/disclosed/used] after/before the priority date of March 26, 1996", render the claims of the "Ominbus" type.

Claims in utility applications that define the invention entirely by reference to the specification are properly rejected under 35 U.S.C. 112, second paragraph, as failing to particularly point out and distinctly claim the part, improvement or combination which Appellant considers his or her invention or discovery. See Ex parte Fressola, 27 USPQ2d 1608, 1610 (Bd. Pat. App. & Int. 1993). In the instant case, Appellant is attempting to define the invention entirely by reference to everything that another's disclosure might not describe (any prior art that might possibly have "disclosed" or "used" CSAIDS for treating an inflammatory disease), which is actually more indefinite (if that is possible) than a traditional "Omnibus" claim.

Anticipation Rejection

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 5, 6, 13 and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Adams et al (USP 5,545,669).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37

CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The prior art uses Applicant's preferred compounds (see and compare the structure given at patent column 4, lines 35 *et seq*. with that given at the top of page 5 of the instant specification) to treat psoriasis (column 23, line 62; see also the penultimate line of claim 14), a condition "characterized by excessive, undesired or inappropriate angiogenesis." The prior art treatments are specifically described as inhibiting 14 kDa PLA2: see column 22, lines 19-60, for instance.

Obviousness-Type Double Patenting Rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5, 6, 13 and 14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 14 of U.S. Patent No. 5,545,669.

Conflicting claim 14 recites the treatment of, *inter alia*, psoriasis (a disease "characterized by excessive, undesired or inappropriate angiogenesis") with the same compounds preferred by Applicant. Accordingly the conflicting claim is specific to, and thus coextensive with, the instant generic claims such that an obviousness-type double patenting rejection is appropriate under the reasoning set forth by Vogel, Goodman and the other precedent cited supra.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick Krass whose telephone number is (571) 272-0580. The examiner can normally be reached on Monday-Friday from 9:30AM to 6:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marschel Ardin, can be reached at (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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